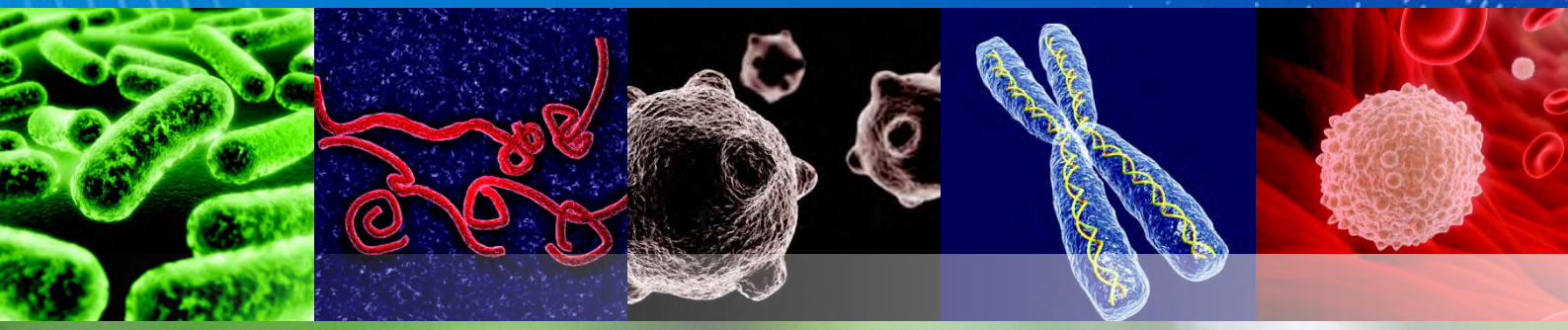
ecetoc

EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS



Annual Report 2012

EUROPEAN CENTRE FOR ECOTOXICOLOGY
AND TOXICOLOGY OF CHEMICALS

Annual Report 2012

Contents

ECETOC AT A GLANCE

Established in 1978, ECETOC is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

ECETOC also provides scientific representation for its member companies through presentations at specialist meetings and by participation in the scientific activities of international agencies, government authorities and professional societies.

A non-profit, non-commercial and non-governmental organisation, ECETOC prides itself on the objectivity and integrity of its work programme, the output of which is published in the form of peer-reviewed reports and articles in peer-reviewed journals, or as specialised workshops.

Purpose

ECETOC's purpose is to develop concepts, data and positions which underpin the use of scientific principles in the translation of policy into regulation in Europe: to enable the benefits of chemicals to be realised while protecting human health and the environment.

Values

ECETOC has strong values of science and integrity; it works by establishing objective positions and then moving forward, not backwards from a predetermined view.

Vision

ECETOC will be the partner of choice focusing and engaging industry expertise for the European Commission, ECHA, and EFSA in the development of practices and concepts based on science as policy becomes embodied in regulations.

Mission

To promote the use of good science in human and environmental risk assessment of chemicals, biomaterials and pharmaceuticals.

Approach

ECETOC pursues its vision and mission through an issue-based science strategy comprising 10 science areas grouped under 5 main themes (see chapter entitled 'Science Programme'):

- **Presence of chemicals in humans**
- **Presence of chemicals in the environment**
- **Effects in humans and ecosystems**
- **Methods**
- **Science of risk assessment**

MEMBERSHIP

Membership benefits

Manufacturers and users of chemicals (and biomaterials and pharmaceuticals) can become either a Full or Associate Member of ECETOC according to the proportion of their turnover derived from chemicals, (see www.ecetoc.org/membership).

Membership of ECETOC demonstrates the practical commitment of a company to the principles of Responsible Care® via their active scientific and technical contribution to initiatives supporting the safe manufacture and use of chemicals, pharmaceuticals, and biomaterials through good science.

The diversity and range of its members' expertise are key ingredients for ECETOC's achievements in the pursuit of this objective. ECETOC's success depends on member company employees being able to dedicate their time to furthering projects within the framework of an ECETOC task force.

In so doing, member company employees benefit from access to a high quality network of scientific expertise and ECETOC is able to leverage this pool of knowledge in order to represent and promote the European chemical industry's science in its relationships with European and international institutions.

ECETOC member companies benefit from being in a position to influence its scientific agenda. They can propose subjects to be tackled by its work programme and can have a representative on its Scientific Committee.

Any member company employee can request a login to the ECETOC members' site: http://members.ecetoc.org where they can download any ECETOC report, keep track of discussions at Scientific Committee level and check the progress of the work programme.

ECETOC Member Companies

At the start of 2013, ECETOC membership comprised the following 43 companies:

*** = Associate member companies**

In January 2013, ECETOC welcomed Sumitomo Chemical as its latest member company. Established in 1913, Sumitomo Chemical Group includes over 100 subsidiaries and affiliates, and operates businesses in five sectors: basic chemicals, petrochemicals, IT-related chemicals, health & crop sciences, and pharmaceuticals.

MESSAGE FROM THE CHAIRMAN

As scientists probe deeper into cellular physiology, new techniques in 'omics and methods to assess epigenetic imprinting present questions such as what is an adverse or transient effect within normal variation. These and other topics are being addressed by ECETOC to ensure there is sufficient knowledge and experience when the time arrives to apply these tools and techniques to enhance current risk assessment practices. While ECETOC looks to the future to provide guidance on realistic risk assessment, its major focus remains directed towards those tactical and immediate issues affecting how risk assessment is used and applied now. Whether addressing tactical or long term strategic topics, there is a need to more effectively use the resources we have and where possible cooperate with strategic science partners.

In 2012, the ECETOC Board agreed to move from being an Administrative body and adopted an operational management model. This has resulted in the Board focusing on two areas - Partnerships and Performance.

The coordination of scientific efforts, even within the relatively narrow arena of risk assessment, poses challenges with independent funding bodies following individual pathways and with resources sometimes being spent on similar or over-lapping activities. The key is for ECETOC to further develop partnerships and cooperation with public and private scientific organisations in order to enhance and improve risk assessment.

The second area is to certify the high-end performance of ECETOC to ensure activities and products meet the requirements of members and stakeholders. With a diverse membership, different stakeholder aspirations and limited resources, it is difficult to be "all things to all men". We will therefore introduce processes to enhance membership engagement in agreeing the ECETOC science portfolio of activities.

These and other developments are however for the future, but now let us reflect on some of the changes and achievements during 2012.

2012 included Dr Alan Poole replacing Dr Neil Carmichael as Secretary General and the Secretariat moving to new offices. There have also been some changes in ECETOC Board membership with Dr Craig Nessel of ExxonMobil Biomedical Sciences succeeding Dr Dick Phillips, and Dr Karen Niven of Shell replacing Dr Tamara Nameroff. The year ended with Sumitomo Chemical Europe agreeing to join ECETOC with membership starting January 2013.

Looking at ECETOC scientific roles, endocrine disruption is still a topic requiring attention since 2008 when ECETOC initiated a task force to develop specific scientific criteria to identify endocrine disrupters in Europe as requested by the European Parliament. In 2009, ECETOC was the first scientific organisation to propose criteria for hazard

identification and characterisation of endocrine disrupters that require special regulatory treatment. Two workshops organised in 2009 and 2011 produced scientific publications outlining approaches for risk assessment of endocrine disrupters. The paper in the series, published in 2012, received an award from US Society of Toxicology as the best paper on risk assessment to be published in 2012. The ECETOC proposals on risk assessment of endocrine disrupters have been presented at scientific fora (EUROTOX, SETAC, EEMS), shared with regulatory authorities, members of the European parliament and European Institutions. As a result, ECETOC was invited to join the Commission's DG Environment Endocrine Expert and Ad Hoc groups discussing various scientific issues surrounding endocrine disrupters.

Another highlight of 2012 was the ECETOC workshop to upgrade the Targeted Risk Assessment (TRA) tool that provides a science based approach to first tier risk assessment under the REACH regulation. This workshop attracted nearly 200 participants again demonstrating the importance of ECETOC work for improving the science of risk assessment. The workshop has resulted in two human health components being incorporated into the new Chesar version 2.

These two examples of scientific leadership stand out among the many activities undertaken by ECETOC and demonstrate that ECETOC is a unique organisation with an exclusive value proposition of developing and interpreting science to produce the knowledge that effective risk management policy requires. Your continued support and participation in ECETOC is encouraged and welcomed.

Martin Kayser
Chairman of the Board of Administration

ECETOC BOARD OF ADMINISTRATION

The Board of Administration is empowered by the Annual General Meeting with the management and administration of ECETOC and delegates these tasks on a daily basis to its Secretary General.

The Board is composed of at least six member company representatives. Two Board members are entitled to represent the Associate members. Board members have a two-year mandate and are responsible for the overall policy and finance of the association. The Board is also responsible for appointing the members of the Scientific Committee. Member companies may propose candidates for the Board; these candidates must have managerial duties within their company and possess scientific and technical experience.

At the 2012 AGM:

The Chairman particularly wished to thank Dr. Neil Carmichael who would be retiring as ECETOC Secretary General at the end of June. His contribution to the association had been invaluable over the past six years and the occasion was marked with the presentation of a gift.

Election of Board Members:

Dr. Julia Fentem (Unilever), Dr. Petra Hanke-Baier (Procter & Gamble) and Mr. Steve Rumford (AstraZeneca) were re-elected to the ECETOC Board, effective immediately.

Dr. Robert Rickard (DuPont SHE & Sustainable Growth Center) was elected as a new member to the ECETOC Board.

ECETOC Board Members (January 2013)

Martin Kayser
BASF
(Chairman)

Steve Rumford
AstraZeneca
(Vice-Chairman and Treasurer)

Julia Fentem
Unilever

Petra Hanke-Baier
Procter & Gamble

Peter Hertl
Syngenta

Thomas Jostmann
Evonik Industries

Tamara Nameroff
Shell

Richard Phillips
ExxonMobil

Robert Rickard
DuPont

Anne Wallin
Dow

REPORT FROM THE SECRETARY GENERAL

The year 2012 was one of change for ECETOC. The first change was moving offices. While the distance was not great, the organisation, packing and unpacking is similar whether moving 40 metres or 4,000 kilometres. The second change was replacing Neil Carmichael upon his retirement as Secretary General, a role in which he had provided leadership and inspiration to ECETOC over the previous 5 years. Both activities were finally accomplished towards the end of the year with my appointment as the new Secretary General and with the last boxes being unpacked in November.

Nevertheless, ECETOC enjoyed another successful and productive year. One of the highlights was a workshop on the upgraded Targeted Risk Assessment (TRA) tools that provide a science based approach to first tier risk assessment for the REACH evaluations. This workshop attracted nearly 200 participants providing further evidence of the important contributions that ECETOC makes to the science of risk assessment. Working in close co-operation with ECHA, the two human health components of the ECETOC TRA have now been incorporated into the new Chesar version 2. The TRA has had, and continues to have, a major impact on how risk assessments for REACH have been conducted. A recently published European Commission (EUROSTAT) study on the impact of REACH has recognised that over 80% of the registrants have used the ECETOC TRA tool when a CSA has been required. The TRAs impact on REACH is self-evident and ECETOC continues to work with ECHA and other groups on further developments to these tools. A second workshop focused on the assessment of environmental persistence and the debate over the regulation of PBT chemicals.

Last year also saw the publication of four ECETOC reports including an extensive review on co-exposures at low doses and one on category approaches that was delivered within a challenging short timeframe. Under the leadership of Neil Carmichael, there was a move towards ECETOC publishing its work in the peer reviewed scientific literature, and consequently in 2012, five articles developed by ECETOC task forces and workshops were published in this way. One of these articles, *Risk assessment of endocrine active chemicals: identifying chemicals of regulatory concern* was recognised by the American Society of Toxicology as the top best paper advancing the science of risk assessment. In addition, other topics covered in these publications were thresholds of toxicological concern, combined chemical exposures, integration of human and animal data in risk assessment and use of ‘omics as a tool to elucidate mechanisms of toxicological action.

The year 2013 will bring its own challenges. As always, there is a need to identify and respond to societal concerns about the health and environmental risks posed by chemical substances. The role of

ECETOC is to promote good, understandable science and weight of evidence approaches as a balance to conjecture and anecdotal evidence. Delivery and translation of science into knowledge for informed business and public policy decisions is a major strength and this remains the focus of ECETOC. As new tools and technologies deliver ever increasing amounts of data, ECETOC provides the organisation to structure and analyse the information required by industry and regulatory communities in a clearheaded and knowledge-based way.

Alan Poole
Secretary General

SCIENCE PROGRAMME

Foreword from the Scientific Committee Chairman

Once again the last year has been an extremely busy and productive year for the Scientific Committee. The political and regulatory climate for chemicals in Europe continues to be very challenging: often increasingly conservative in its approach to new guidelines and identification of new issues or questions. Responding to this challenge is significantly increasing the demand on ECETOC for new task forces and workshops to investigate or address these issues. This translates into real pressure on the member companies to find sufficient and appropriate expertise to contribute to these ECETOC activities while facing increasing internal workload demands with REACH and other regulatory initiatives. One of the key challenges for the Scientific Committee has been to balance this resource issue, i.e. how any new activity needs to be prioritised against important existing activities on ECETOC's portfolio of projects and with a view on available resources. This is a process which will need increased focus and management in future years.

Having said this, over the past year the Scientific Committee has made considerable progress on some key areas of the ECETOC science strategy - both in terms of new task forces / workshops, as you will see in this report, as well as continued engagement on some key longer term issues. For example, the on-going EU debate on the potential impact of endocrine disrupting chemicals continues to be a major concern. There have been a number of meetings where ECETOC has continued to build on the work of recent task forces and workshops to promote a risk based approach. ECETOC proposed a meeting involving the key experts from academia, industry and regulators to better understand endocrine disrupter low doses effects. The purpose was to gather individual scientists who are committed to look at the various topics scientifically and draft a research programme with clear steps on what kind of research is needed to address any open questions. This proposal was presented at the EU Ad Hoc meeting on endocrine disrupters and received a good response; it was thought that the outcome of such a meeting could be taken into account in EU policy discussions. This initiative also received good feedback from academia who felt that it gives the opportunity to those with opposing views to present their opinions and come to a conclusion. The meeting took place in April 2013 in Barcelona, Spain and will be covered in more detail by the 2013 Annual Report.

Activities in Europe continue to highlight the concerns over presence and potential impact of chemical combinations in the environment, along with the perception that current risk assessment procedures are inadequate. The report of the ECETOC task force on low-dose interactions was issued at the end of 2012; it was widely

acknowledged as an excellent overview of the available science in this area.

A number of task forces and workshops have been proposed / initiated during the reporting year which cover the breadth of the ECETOC scientific strategy and illustrate the wide range of issues currently challenging the Scientific Committee. New proposals for task forces range from: *Developing guidance for effective use of human exposure data*, to *the use of Ecosystem services in chemical risk assessment*; from *the use of Read-across for nanomaterials* to *Respiratory sensitisation* to *the Adequacy of current C&L system for environmental hazards*. Additionally, in February 2013, ECETOC ran workshops on *Mode of Action: Recent developments, regulatory application and future work*, and *'Omics and risk assessment science*. A further workshop on *Species Sensitivity Distribution* is in preparation.

There have been changes to the membership of the Scientific Committee. In February 2013 we were pleased to welcome Peter Boogaard from Shell to the Committee. Peter has been a long term contributor to ECETOC through task forces and workshops and is a strong addition to the science base of the committee. By the year end, there were also two resignations from the Committee; David Farrar due to retirement, and Gerard Swaen due to job change. Both individuals are greatly acknowledged for their active participation and contributions made over many years. With the number of changes to the committee over the past couple of years, we thought that this was an opportune time to assess whether the areas of expertise covered by SC members still reflected what was needed, given the ever changing external drivers in health and environment. We reviewed our last survey for the key topic areas we felt were relevant and then asked the current SC members for their distribution of expertise to evaluate key gaps we believe should be addressed before any decision on further additions to the SC.

Finally, sadly this will be my last contribution to the Annual Report as I am stepping down as Chairman of the Scientific Committee. It has been a great privilege to lead this group for the last 3 years but pressure of work at Syngenta means I cannot dedicate sufficient attention to carry out this important role. I would like to take this opportunity to thank the members of the Committee, and the staff of the Secretariat, for their help and support without which the job of the Chairman would be impossible. I believe ECETOC has a unique place to promote the use of good science in the assessment of safety of chemicals and maximising this opportunity will be the challenge for the Scientific Committee going forward.

Fraser Lewis, Syngenta
Chairman of the Scientific Committee

Science Programme

Highlights of 2012

Completed task forces

Targeted Risk Assessment

Strategic Science Areas: Integrated testing strategies, Risk, hazard and precaution

REACH, the EU regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals, entered into force in June 2007 to streamline and improve the former legislative framework on chemicals of the EU. One of the key challenges of REACH is that it envisages the registration and evaluation of approximately 30,000 chemicals by producers and importers. Many of these chemicals will be classified and will require Chemical Safety Assessments to support their registration. Faced with such a challenge, both practically and scientifically, suitable tools that are accessible to non-experts are a key need of the REACH process.

To achieve these aims, ECETOC developed a tiered (step by step) approach for calculating the exposure to and risks from chemicals that might reasonably be expected in defined circumstances of use. The approach addresses exposure to consumers, workers and the environment. The general concept of ECETOC's Targeted Risk Assessment (TRA) is based on the premise that, by making suitably conservative assumptions, broad exposure/risk models can be applied to determine where any further detailed assessment of risks may be required.

Since its launch in 2004, the TRA Tool has proved to be an overwhelming success. Since the release of the TRA version 2 (TRAv2) in July 2009, over 15,000 downloads of the tools have been made and many major consortia placed the TRA at the heart of their REACH Registrations.

Following the 2010 registrations, the core group of the TRA task force sought feedback from users of the tool in order to identify areas where its functionality and accuracy might be further improved. At the same time, ECHA signalled its intent to update its Chesar CSA/ES tool. In this respect, updates to the worker and consumer tools have been developed in close co-operation with ECHA, who have incorporated the two human health components of the TRA into the new Chesar version 2. In addition to these two components, a spreadsheet implementation of EUSES is included in the integrated part of the TRA to facilitate environmental assessments. The integrated part of the TRA has also being updated. These new versions have been tested against the TRAv2 and other exposure models.

The new TRAv3 was launched in April 2012 together with updated user guides to reflect the changes, and in July 2012 further guidance was published in Technical Report no. 114: *ECETOC TRA version 3: Background and Rationale for the Improvements*. This and previous TRA reports can be downloaded free of charge from the ECETOC website: http://www.ecetoc.org/tra

Low-dose interactions

Strategic Science Area: Mixtures and co-exposure

Chemical risk assessment is predominantly carried out on individual substances, and this is also reflected in most chemical-related legislation. In reality though, humans, fauna and flora are exposed to a variety of substances concurrently. The toxicology of chemical mixtures is usually addressed through concepts of concentration or dose addition and independent action; synergism is considered to occur only rarely.

More recently, the question arose whether such risk assessment procedures are adequate for assessing combined exposure to multiple chemicals. Much attention is being given to the so-called 'cocktail effect' which is hypothesised to occur due to simultaneous exposure to low levels of environmental chemicals. According to this theory, unexpected effects can occur due to interaction in the body between these chemicals, even though the levels could be below the threshold of toxicity for the individual chemicals or their breakdown products. It is claimed that these interactions at low-dose levels may be greater than additive.

An ECETOC Task Force undertook an extensive literature search looking for evidence of such effects at environmental concentrations and multiples thereof, in mixtures tested at or near the NO(A)EL of their single components, and in mixtures tested well below the NO(A)EL of their single components.

The findings were published in July 2012 in Technical Report no. 115: *Effects of Chemical Co-exposures at Doses Relevant for Human Safety Assessments.*

The report can be downloaded free of charge from the ECETOC website. Direct link to summary and PDF download: http://bit.ly/ecetoc-tr115

Category approaches, read-across, (Q)SAR

Strategic Science Area: Integrated testing strategies

An accepted practice for the assessment of human health and environmental safety of chemicals is the use of models and analogues to fill data gaps for specific endpoints either for single or multiple chemicals that share structural similarities, and/or comparable reactivity or similarities in metabolism in mammals, fish and other organisms. For example, this approach is acceptable, with limitations, in preparing dossiers for REACH, and it supports efforts for reducing animal testing. The OECD has published guidance on the formation and use of chemical categories for data gap filling. In December 2010, an ECETOC task force produced TR 109: *High information content technologies in support of read-across in chemical risk assessment*, a project that has highlighted methods for read-across.

With the plethora of models and guidance growing for both human health and the environment, it would be prudent to identify recommended practices. Additionally, the 2013 and 2018 REACH deadlines are pending; these deadlines require lower volume producers and importers to submit chemical safety assessments. A report describing recommended practices in this area would be useful in supporting industry's risk characterisation and prioritisation activities across all sectors. To this end, an ECETOC task force of industry and regulatory experts on categorisation methods, read-across and the use of (Q)SAR in risk assessment has prepared Technical Report no. 116: *Category approaches, read-across, (Q)SAR*.

The report can be downloaded free of charge from the ECETOC website. Direct link to summary and PDF download: http://bit.ly/ecetoc-tr116

Science Programme • Highlights of 2012

Task forces established

Mode of action and identification of adverse versus non-adverse effects

Strategic Science Area: Integrated testing strategies

The scientifically sound discrimination between adverse and non-adverse effects has always been a key element in the evaluation of toxicological results. ECETOC's Task Force 'Recognition of, and differentiation between, adverse and non-adverse effects in toxicology studies' (TR85) has addressed this issue principally in terms of classical biochemical and histopathological endpoints.

However, over the last several years, new technologies (principally 'omics) are being used to explore toxicological mechanisms through changes of unknown relevance to harmful outcomes. While there is an accepted regulatory tradition in distinguishing observable effects of toxicological significance from those which are not considered adverse, this convention does not yet exist for these new technologies.

This topic was also prioritised at the ECETOC 'Science Needs for REACH' workshop that took place in March 2011. Industry could make use of advice on the interpretation of studies with the new technologies when substance evaluations are being discussed with ECHA. Therefore, a Task Force was established to describe how understanding 'mode of action' may be relevant to the definition of adverse and non-adverse effects and what contribution the new (omic) technologies may make to this.

Science Programme • Highlights of 2012

Workshops

Science Programme • Highlights of 2012• Workshops

TRA Tool version 3 - public workshop

3 May 2012, Brussels, Belgium

Strategic Science Areas: Integrated testing strategies, Risk, hazard and precaution

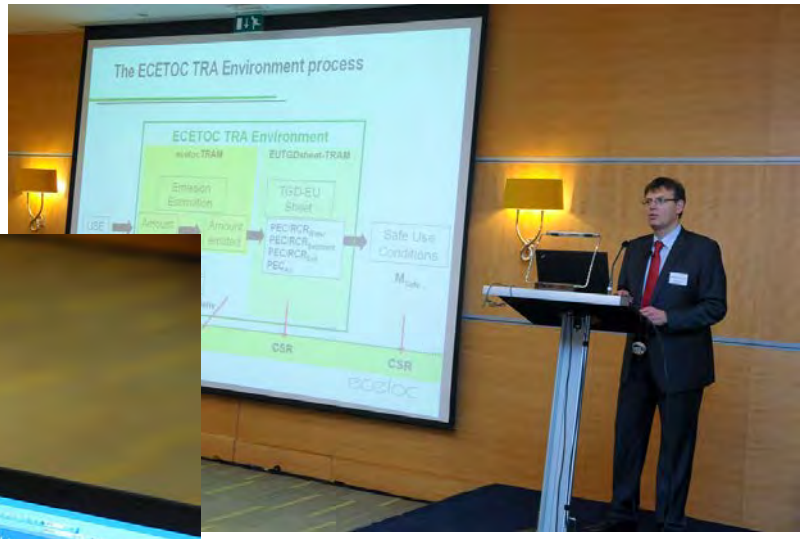
The ECETOC Targeted Risk Assessment (TRA) tool was launched in 2004 and consists of 3 separate models for estimating exposures to workers, consumers and the environment that arise during a series of events ('exposure scenarios'). In order to ensure that the TRA fully aligned with the expectations contained in Chapters R12-R16 of the Technical Guidance on Information Requirements and Chemicals Safety Assessment (IR&CSA), ECETOC released version 2 of the TRA in 2009 (TRAv2).

Following the completion of Phase 1 of REACH in December 2010, ECETOC approached users of the TRA to seek their ideas for how the TRA might be further improved. The aim of this exercise was to ensure that key learnings arising from the use of the TRA in 2009/10 could be captured into an updated version that would be available for use in Phase 2 of REACH. The intention was not to radically overhaul the TRA, rather to further improve its accuracy and flexibility, within its existing framework.

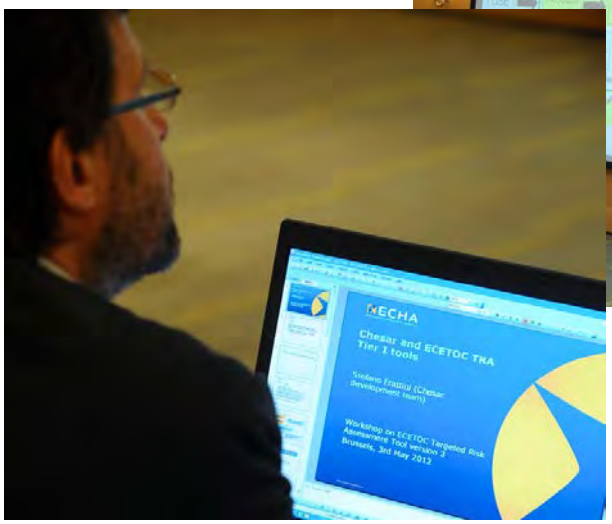
Thus, in April 2012, ECETOC launched TRAv3 together with updated user guides. The Tool is available in two forms: as an integrated exposure/risk assessment tool covering worker, consumer and environmental exposures; and as a standalone consumer exposure estimation tool. Both forms of the TRA are downloadable from the TRA website without charge, together with their supporting user guides which include Technical Report no. 114: *ECETOC TRA version 3: Background and Rationale for the Improvement*, which was published in July 2013. The report can be downloaded free of charge from the ECETOC website. Direct link to summary and PDF download: http://bit.ly/ecetoc-tr114

ECETOC has been working with the European Chemicals Agency (ECHA) as part of its work activities associated with the delivery of a revised version of the Chesar Chemical Safety Assessment tool (http://chesar.echa.europa.eu/). The new version of Chesar was released in June 2012 and is intended to directly reflect version 3 of the TRA for both worker and consumer exposures. Furthermore, Chesar v2 allows the incorporation of the Specific Environmental Release Categories (SpERCs) that are included as a key element of the environmental component of the TRAv3.

With nearly 200 participants, the workshop was one of the largest that ECETOC has organised



Johannes Tolls (Henkel) presented environmental exposure assessments, SPERC and SCED



Stefano Frattini of the Chesar development team presented an overview on Chesar and ECETOC TRA Tier 1 Tools

Assessing Environmental Persistence

6-7 November 2012, Paris, France

Strategic Science Area: Assessment of environmental fate and behaviour

Tom Federle (Proctor & Gamble) speaking on the challenges of assessing degradation and persistence

The workshop was organised and co-sponsored by ECETOC and the CEFIC LRI ECO 11 project, co-organised by representatives from ECETOC, Federal Environment Agency of Germany UBA and the Environment Agency (EA) of England and Wales, and took place at Les Salons France-Amérique, Paris, France. This is a follow up to an initial 2007 workshop which ECETOC held to assess areas of research required to help develop the scientific understanding of factors that affect the persistence of chemicals in the environment. The 2007 workshop on "Biodegradation and Persistence" was co-hosted by ECETOC and the Environment Agency (EA) of England and Wales and held at Holmes Chapel in the United Kingdom. Attendees from academia, regulatory agencies and industry discussed the challenges and uncertainty faced with persistency assessments at the screening and confirmatory testing level.

The primary aim of the 2012 workshop was to:

- Identify whether / how the programmes initiated as a consequence of the Holmes Chapel Workshop have helped further the understanding of biodegradation / persistence related issues,
- Identify and prioritise key areas for further future research.

A Workshop Report on the outcome of the discussions is currently being finalised and will shortly be published as Workshop Report no. 24: *Assessing Environmental Persistence. 6-7 November 2012, Paris*

Science Programme • Highlights of 2012

Symposia and other meetings

2012 Annual Technical Meeting on *Exposure in Risk Assessment*

6 June 2012, Brussels, Belgium

For the 2012 Annual Technical Meeting (ATM), ECETOC chose to bring forward the topic of 'Exposure'. Looking at the hazard-side of risk assessment, test methods are already well-developed, and continue to be improved, and a large pool of chemical-specific data available. But exposure is often somewhat orphaned. The programme of the 2012 ATM, '*Chemical Exposure for Risk Assessment: Present Problems and Future Solutions*', brought together enlightening speakers and stimulated an insightful debate. The lunchtime poster session provided time for networking amongst participants.

The meeting started with the keynote speech by José Tarazona of ECHA on the importance of exposure assessment, in particular under REACH and the CLP regulation. He reviewed how exposure is applied in the chemical registration and evaluation steps, and described how exposure scenarios are being defined through the use descriptors, operational conditions and risk management measures. He also pointed out where he sees the current specific needs to improve exposure assessments, namely on refined methods and tools to address aggregate exposure to multi-constituent and UVCB substances, as well as to address combined exposure to different substances. Thereby, it was important to understand realistic exposure and co-exposure levels.

Gerard Swaen (Dow) - one of four speakers covering 'the present'

Four speakers covered 'the present'.

Gerard Swaen *(Dow)* gave his thoughts about 'exposure as a limiting factor in epidemiology research' mainly due to poor quality data on exposure.

Andrew Sweetman *(Lancaster University)* addressed 'environmental persistence and exposure assessments' showing that regulatory approaches can present an unrealistic scenario by only looking at single media degradation half-lives.

Kim Travis *(Syngenta)* spoke about the work of the recently completed task force on 'combined exposures at low doses' whereby exposure concentrations played a critical role, which is often not the case in mixture toxicology.

Marike Kolossa *(German UBA)* presented current bio-monitoring projects in Germany that are designed to establish 'real' environmental exposure levels to priority pollutants.

Tim Pastoor, one of four speakers covering 'the future' and Fraser Lewis, both of Syngenta

'The future' was addressed by another four speakers.

Jonathan Goodman *(Cambridge University)* in his talk on 'chemical informatics for risk assessment' showed how molecular information can provide valuable data for toxicology and for an understanding of exposure.

Tim Pastoor *(Syngenta)* provided an overview of the Risk 21 project that, amongst other topics, postulates the paradigm shift in risk assessment whereby problem formulation begins with exposure estimates rather than toxicity hazard data.

Sylvia Jacobi *(Albemarle)* reviewed the work of another recently completed task force on risk assessment of PBT which described refined methods for their exposure assessments and also identified further research needs.

Jacqueline van Engelen *(RIVM)* talked about methods and databases to 'understand the nature of consumer exposures to mixtures' and where information needs still lay.

Finally, participants from industry (member and non-member companies), academia and governmental research institutes discussed in two breakout groups where they see research needs to advance exposure science towards improving human and environmental risk assessment. Constructive broad ideas for new activities that ECETOC (or LRI) could undertake emerged. These were further discussed within the ECETOC Scientific Committee to distil specific project proposals.

2012 Environment Progress Review

28/29 February 2012, Brussels, Belgium

In February, the environment progress review meeting took place with a large turn-out of 29 scientists. This annual meeting sets out to inform and review the spectrum of ECETOC environmental activities, task forces, workshops and LRI projects.

The second day of the meeting focussed on identifying new ideas for ECETOC and Cefic LRI activities

Dose-response relationship and receptor-mediated toxicology

20 June 2012, Stockholm, Sweden

A session on **'Dose-response relationship and receptor-mediated toxicology'** was organised by ECETOC for the programme of the 2012 EUROTOX congress. Under Remi Bars' *(BayerCropscience)* and Ben van Ravenzwaay's *(BASF)* chairing, five speakers shared the outcome of studies with nuclear receptors, such as CAR/PXR, PPAR, ER, AR, mediating various forms of toxicity.

- Earl Gray *(US EPA)*: Endocrine toxicity mediated through ER, AR steriodogenic and AhR pathways. Case studies and dose-response relationship

- Russell Thomas *(Hamner Institutes for Health Sciences)*: Genomic dose-response modelling to inform key events in a mode-of-action risk assessment

- Remi Bars *(BayerCropscience)*: Endocrine toxicity-mediated through the AR and evaluation of dose-response relationship

- Cliff Elcombe *(CXR Biosciences)*: Dose-response relationship toxicity in CAR/PXR humanised mouse

- Dieter Schrenk *(University Kaiserslautern)*: Dose-response relationship in toxicity following Ah receptor activation in animal models

This topic addresses an on-going debate which is controversial when exploring the nature of the dose-response curve and the effect at the low end of this curve. The concept of threshold in receptor-mediated toxicity is currently being challenged, particularly in the field of endocrine toxicity. The latest research in the field presented made a valuable contribution to this debate witnessed by the sizeable audience in this session and that engaged in a lively debate.

EUROECOTOX: Further steps on the Replacement, Reduction and Refinement (3Rs) of Animal Experiments in Ecotoxicology

28-29 June 2012, Dübendorf (Switzerland)

Current chemical risk assessment and effluent and water quality monitoring require ecotoxicity testing using vertebrates, in particular fish, amphibians and birds. Due to increased ethical concerns, the development and acceptance of alternative methods is timely. To this end, the "1st European Conference on the Replacement, Reduction and Refinement of Animal Experiments in Ecotoxicology" was successfully carried out in Dübendorf (Switzerland). The conference was organised by EUROECOTOX, a coordinating action funded by the European Community's Seventh Framework Programme, in which ECETOC is a partner.

The conference provided a good platform for young scientists and experts from academia, industry and regulation in the adoption of the 3Rs principles for animal test uses in environmental scientific experimentation and risk assessment. It focused on the current state and future directions of the development, implementation and application of the 3Rs, from bench to acceptance. An exciting programme was put in place based on invited key note speakers and presentations from submitted abstracts. A special key note lecture was given by Susanna Louhimies (DG Environment, European Commission) about the establishment of the 3Rs in European Legislation. About 62% of participants were from academia, 22% from industry and 16% from regulators and other stakeholders.

The conference had different outcomes when aiming to identify where we stand and what barriers need to be overcome in order to turn the 3Rs principles in ecotoxicology into practice, especially concerning five areas: (I) experimental approaches, (II) towards integration and implementation, (III) establishing the 3Rs in European legislation (IV) perspectives and initiatives towards the 3Rs, and (V) computational approaches a final plenary discussion about the future of alternative methods in ecotoxicology. A short summary of the conference, programme and abstracts is available from EUROECOTOX DOCUMENTS on the project website.

Group photo at the conference

The event was co-funded by the European Society of Toxicology in Vitro (ESTIV), who sponsored the participation of ESTIV members and gave two prizes for young scientist's presentation and poster.

For more information on EUROECOTOX, the network, major goals and activities and on how to join the network, please visit the website:
http://www.euroecotox.eu

Symposium on "Epigenetics and chemical safety"

7 September 2012, EEMS annual conference, Warszawa, Poland

The symposium was jointly organised by ECETOC & EEMS and held on the first day of the EEMS meeting. It was supported by funding from CEFIC-LRI. In his introduction, Ben van Ravenzwaay *(BASF, Germany)* referred to the Rome ECETOC workshop (WR 23) on which this symposium was based. There followed six invited presentations, which were well received:

An overview of where "Toxicology meets epigenetics", presented by Jay Goodman *(Michigan State University, USA)*. He stressed that there are numerous fundamental issues that must first be addressed before incorporating an epigenetic evaluation into toxicity/safety assessment. For example, which aspect(s) of epigenetics will be monitored; what methodology(ies) will be used; what biological endpoint(s) will be evaluated; what model system(s) and compounds might be employed? Goodman concluded that it is not the time (yet) to incorporate an epigenetic evaluation into safety assessment.

Mohamed Benahmed, *INSERM (Institut National de la Santé et de la Recherche Médicale, Nice)* spoke about "µRNAs and epigenetics". He had examined whether endocrine disrupting chemicals (EDCs) induced their adverse effects via epigenetic modifications, with a focus on µRNAs , i.e. non-coding RNAs that regulate gene expression by targeting messenger RNAs (mRNAs). µRNAs have fundamental roles in cellular responses to xenobiotic stresses, which affect a large range of physiological processes such as development, immune responses, metabolism, tumour formation as well as toxicological outcomes. Benahmed showed results from different *in vivo* and *in vitro* models suggesting that EDCs may affect µRNAs expression and function.

The potential of chemicals to cause epigenetic alterations was reviewed by John P Thomson *(Medical Research Council, Human Genetics Unit, Edinburgh, UK & MARCAR consortium)*. To elucidate altered DNA modification and covalent histone modifications that may take place at the earliest stages of carcinogenesis, the MARCAR consortium had evaluated the sensitivity and specificity of genome-wide epigenomic and transcriptomic profiling in phenobarbital-treated B6C3F1 mice, a well-characterised rodent model for non-genotoxic liver carcinogenesis. The MARCAR data demonstrated the utility (sensitivity and specificity) of integrated epigenomic and transcriptomic profiling for elucidating early mechanisms and biomarkers of non-genotoxic carcinogenesis.

Sylvain Guibert, *University of Strasbourg, CNRS (Centre National de la Recherche Scientifique, France)* reported on a study of DNA methylation in early embryogenesis

using mouse primordial germ cells. The results showed that the extent of DNA methylation erasure is more complete than in pre-implantation embryos. Very rarely, there is a potential, for transgenerational transmission of DNA methylation over multiple generation in mice. Guibert was applying epigenome mapping to identify abnormal DNA methylation patterns in mouse models exposed to endocrine disruptors (EDs). EDs may induce abnormal DNA methylation marks in germ cells of exposed embryos, and these epigenetic alterations may persist in the subsequent generations.

Jean Cadet *(CEA, Grenoble)* presented results of recent investigations on "TET3 enzymatic oxidation of 5-methylcytosine, 5-hydroxymethylcytosine and 5-formyluracil". 5-Methylcytosine (5mC) that is involved in epigenetic regulation is susceptible to oxidation by enzymatic reactions giving rise to 5-hydroxymethylcytosine (5hmC) among other degradation products. As a novel epigenetic marker, the presence of 5hmC has been recently detected at high levels in the DNA of brain and embryonic stem cells. It was found that the formation of 5hmC in nuclear and mitochondrial DNA of mammalian cells is mediated by the 'ten eleven translocation 1' (TET1) enzyme. Removal of 5hmC is a necessary step and several possibilities have been proposed for the overall demethylation reaction. These were reviewed at the meeting.

Epigenetics in an ecotoxicological context was the subject of the last talk by Michel Vandegehuchte *(Ghent University, Belgium)*. Environmental exposure to e.g. metals, persistent organic pollutants or endocrine disrupting chemicals has been shown to modulate epigenetic marks such as DNA methylation, not only in mammalian cells or rodents, but also in environmentally relevant species such as fish or water fleas. The associated alterations in gene expression often lead to modifications in the affected organism's phenotype. Epigenetic changes can in some cases be transferred to subsequent generations, as demonstrated in water fleas exposed to the epigenetic drug 5-azacytidine. This way, populations can experience the effects of their ancestors' exposure to chemicals, which has implications for environmental risk assessment.

In conclusion, Jos Kleinjans *(University of Maastricht, Netherlands)*, who closed the meeting, pointed out that epigenetics maintain crucial cell functions, seem very complex and dynamic, and may therefore be easily perturbed by toxic chemicals *in vitro*, in animal models and in humans. Understanding such perturbations may profoundly increase our insights into toxic mechanisms-of-action, and lead to the development of better (biologically plausible) predictors of human safety. It would be of particular interest to investigate whether chemically induced changes in such mRNA and µRNA interactions may be irreversible. The challenge is then to apply these insights and extrapolate from *in vitro* to *in vivo* (animal) models to human safety models.

The presentations at the symposium will be published as a special issue of Mutation Research (Elsevier).

SCIENCE AWARDS

With the objective of recognising talented young scientists, ECETOC has been active in the provision of an annual Science Award to outstanding works of science since 2003. The 1st Science Award was accorded on the occasion of its ECETOC's 25th Anniversary to recognise the achievements of three promising European investigators in the fields of science relevant to its mission of supporting the safe manufacturing and use of chemicals, pharmaceuticals and biomaterials through good science. Since then, the format of the Award may have varied but the objectives have remained the same.

In 2012 ECETOC sponsored the following awards for young scientists and is proud to announce this year's winners:

Exposure science related award

Katleen de Brouwere was presented with her award by Chris Money (ExxonMobil)

The ECETOC 'young scientist' award at X2012 (7th International Conference on the Science of Exposure Assessment, organised by the British Occupational Hygene Society) was awarded to Katleen de Brouwere from Vito in Belgium for her paper 'mechanistic risk assessment of indoor air pollutants: exposure to

phthalates'. Katleen successfully applied the methodology developed in the context of TAGS by Dr Alberto Gotti and Dr Spyros Karakitsios of CERTH (GR). The X2012 jury all agreed that Katleen's paper was of a very high standard and that the concepts she addressed (which arise from the Cefic LRI supported TAGS project) take the science of multi source, multi pathway consumer exposure and risk assessment to a new level. Indeed there was much subsequent discussion on how the concepts might also be applied to worker and environmental exposures.

Environmental science related award

The ECETOC Best Platform Award honours the early career scientist with the best platform presentation at the SETAC Europe Annual Meeting. The award winner receives a free registration to the next SETAC Europe Annual meeting and travel and accommodation support. The winner also receives a free SETAC membership. This year's Best Platform Award has been awarded to Dorothea Gilbert, Aarhus University, Denmark, for her talk entitled: *Passive dosing under the microscope reveals that microorganisms enhance the mass transfer of hydrophobic organic chemicals*.

Abstract available via: http://bit.ly/ecetoc-ysa2012-gilbert-abstract

Human health science related award

This is a Best Poster Award for toxicological research into mechanisms and risk assessment, selected by a panel in which ECETOC participates. The winner receives a monetary prize and a free invitation to the following year's EUROTOX meeting. This year's Young Scientist Award on human health sciences, presented at the EUROTOX annual meeting in Stockholm, Sweden, has been awarded to Camille Béchaux, Anses France for her poster presentation on: *Dynamical modeling of dietary exposure to dioxins and corresponding present and future health risk: A case study in France*.

For more details, visit http://www.eurotox.com/sub/eurotox.com/images/awards/2012_eurotox_awards.pdf

LONG-RANGE RESEARCH INITIATIVE

Since 1996, the Long-range Research Initiative (LRI) Programme of Cefic, the European Chemical Industry Council, has been providing proactive scientific data on which the entire industry and regulatory bodies can draw to address societal concerns on a reliable basis.

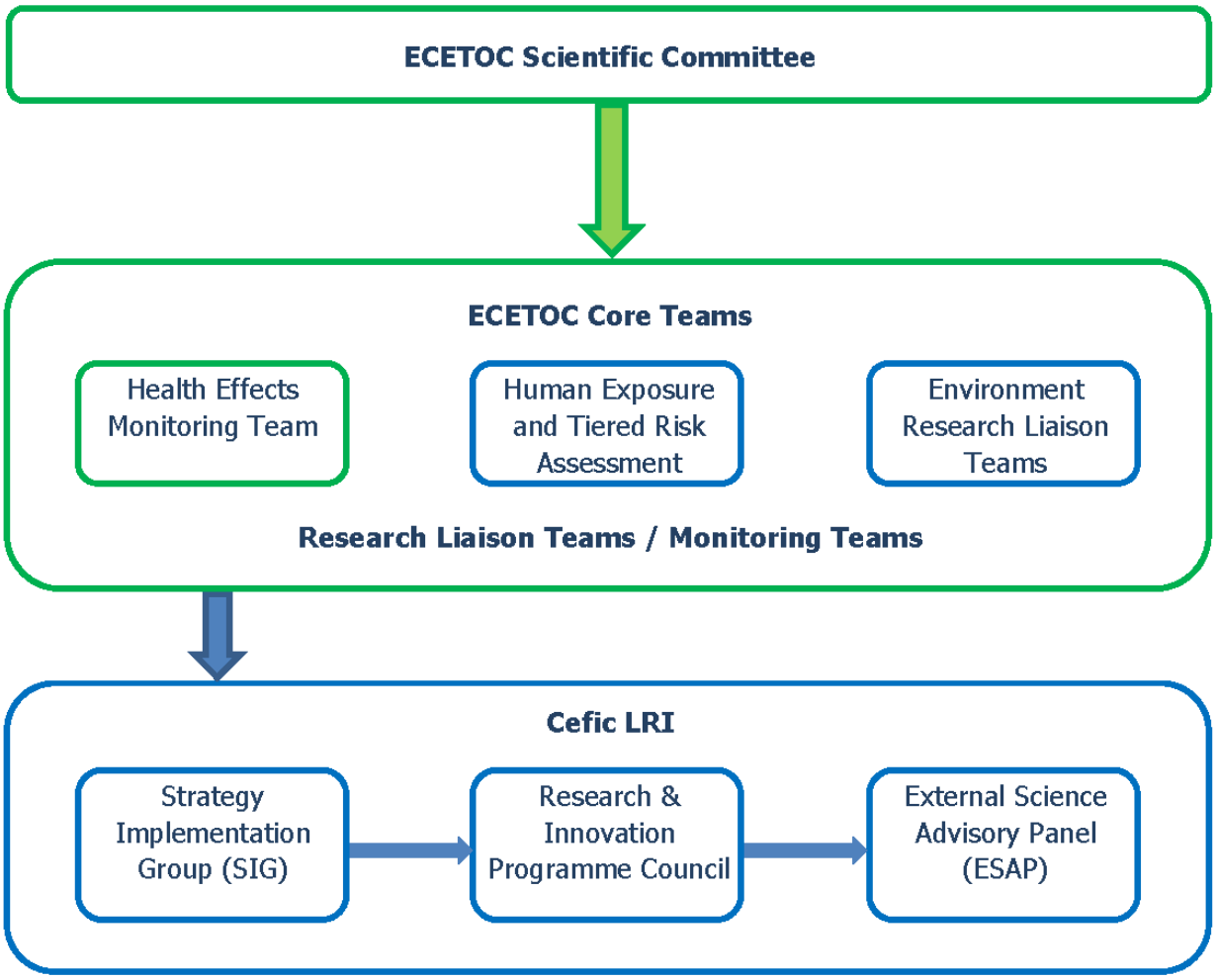
As a fundamental basis for a sustainable chemical industry and a complement to Responsible Care, LRI presents a research programme that is forward-looking and ambitious, but also realistic and coherent. LRI invests in long-term research and delivers transparent, quality-assured scientific data, open to the broad public.

The current research areas of the LRI are addressing key public concerns:

- Development of intelligent testing (including alternatives to animal testing)
- Understanding the effects of chemicals in complex environments
- Public acceptance of new technologies

ECETOC has been the scientific partner to CEFIC LRI from the earliest stage of the process. ECETOC provides scientific support into the LRI, and input into the Research Programme. Within the LRI, ECETOC has the responsibility of maintaining three 'core teams' consisting of industry scientists, who manage the scientific evaluation of applications for funding, recommend the best research proposals and monitor of the progress of selected LRI projects. In particular they are responsible for the:

- Development of topics for research to be considered by the LRI Strategy Implementation Group (SIG). (A core team may organise a workshop with academic, government and industry scientists for this purpose.)
- Drafting of 'requests for proposals' (RfPs) based on ideas submitted by CEFIC and ECETOC stakeholders in the LRI process.
- Setting up selection teams of industry and external experts to choose the best research proposals in response to published RfPs and making recommendations to LRI SIG concerning the funding of the proposals.
- Establishment of scientific liaison with the selected institutions and monitoring the scientific quality and progress of the projects.



Structure of ECETOC support for Cefic LRI

Long-range research initiative

Health Effects Monitoring Team (HEMT)

One new project was initiated by the HEMT in 2012 with the support of specially recruited selection teams (below marked with *). The current research portfolio under the health effects programme, monitored by the HEMT, looks as follows (arranged by strategic theme of the LRI programme):

Intelligent testing strategies

B6: A toxicogenomic approach to enhance the specificity and predictive value of the murine local lymph node assay
Principal investigator: Dr. Darrell Boverhof, Dow, Midland, MI, USA

Acceptance of new technologies and products

N1: Tiered approach to testing and assessment of nanomaterial safety to human health
Principal investigator: Dr. Otto Creutzenberg, Fraunhofer Institute of Toxicology and Experimental Medicine, Hannover, Germany

N3: Towards standardized testing guidelines (reproductive toxicity) relevant to nanomaterials
Principal investigator: Dr. J.J.M (Han) Van de Sandt, TNO, AJ Zeist, Netherlands

AIMT2: Mechanism-based characterisation of systemic toxicity for RepDose database substances employing in vitro toxicogenomics
Principal investigator: Dr. Rob H Stierum, TNO, AJ Zeist, Netherlands

AIMT3: Data-integration for endpoints, cheminformatics and omics
Principal investigator: Dr. Joost van Delft, Maastricht University, Netherlands

Impact of complex environments on health

EMSG49: Reprogramming of DNA methylation during mammalian development and environmental impact of endocrine disruptors
Principal investigator: Dr. Webber Michael, Institute of Molecular Genetics, Montpellier, France

EMSG56: Combined low-dose exposures to anti-androgenic substances
Principal investigator: Dr. Steffen Schneider, BASF, Ludwigshafen, Germany

B10: Animal and human NOAELs: cross-species comparison, inference and synthesis
Principal investigator: Dr. Lesley Rushton, Imperial College London, UK

EMSG57: Endocrine disruptors and obesity, diabetes and heart disease: State of the science and biological plausibility (*)
Principal investigator: Dr. Judy LaKind, LaKind Associates, Catonsville, MD, USA

Long-range research initiative

Human Exposure and Tiered Risk Assessment Monitoring Team (HETRA)

The HETRA team achieved steady progress during the reporting year. A list of all ongoing HETRA project activities in 2012 is given below, conveniently grouped into four traditional areas of exposure/risk assessment science. The HETRA project monitors showed satisfaction with progress made, and the researchers completed four projects (specified below). Furthermore, at its meeting in October 2012, a HETRA selection team aided by outside scientists agreed to recommend three new research proposals for LRI funding (marked with * below). Since the LRI SIG accepted the recommendations and LRI management swiftly concluded the contracts, the new projects were ready for a good start by the year end.

Better characterisation of actual exposures

B4: Integrated exposure for RA in indoor environments (completed)
Principal investigator: Prof. Matti Jantunen, THL (Institute for Health and Welfare), Environmental Health, Kuopio, Finland

B11: Integrated exposure for RA in indoor environments (*)
Principal investigator: Assoc. Prof. Dimosthenis Sarigiannis, Centre for Research and Technology Hellas, Thessaloniki, Greece

B13: Development of a mechanistic in silico multi-scale framework to assess dermal absorption of chemicals (*)
Principal investigator: Prof. Gerald Kasting – University of Cincinnati, OH, USA

Tiered approaches to risk assessment

B8: Improvement of the TTC concept for inhalation exposure and derivation of thresholds with the database Repdose (completed; final report in 2013)
Principal investigator: Dr. Sylvia Escher, Fraunhofer ITEM, Hanover, Germany

Nature of determinants of human exposure

B5: Realistic estimation of exposure to substances from multiple sources (completed)
Principal investigator: Prof. Anastasios Karabelas, CERTH, CPERI, Thessaloniki, Greece

B7: Determining the nature of chemical substance additively from household consumer products
Principal investigator: Dr. Natalie von Götz, ETH, Safety & Environmental Technology Group, Zürich, Switzerland

B9: Characterising the nature of dermal exposure from consumer products and articles
Principal investigator: Ir. Rudi Torfs, VITO (Flemish Institute for Technological Research), Mol, Belgium

B12: Assessing the relevance of the dust contribution to substances from consumer products and articles (*)
Principal investigator: Dr. Natalie von Götz, ETH, Safety & Environmental Technology Group, Zürich, Switzerland

Role of biomarkers

HBM3: Structured data acquisition via in vitro metabolism screens to enhance computational tools (completed)
Principal investigator: Dr. Bas Blaauboer, IRAS, Utrecht, Netherlands

HBM4: Understanding inter- and intra-individual variability in HBM spot samples
Principal investigator: Dr. Ir. Roel Smolders, VITO, Mol, Belgium

Long-range research initiative

Environment Research Liaison Teams (ERLT)

Three new ERLT projects secured funding and were initiated in 2012 with the support of the research liaison teams (below marked with *). Three other projects were successfully finalised as noted below. The current research projects under the ERLT look as follows (arranged by strategic theme of the LRI programme):

Intelligent testing strategies

ECO 8.3: Fish cell line & embryo assays: follow up to the CEllSens ECO8/8.2 project (completed). A Round-Robin test of the RTgill-W1 cell line assay has now been established
Principal investigator: Prof. Kristin Schirmer, Eawag, Switzerland

ECO 9: Investigating the environmental relevance of laboratory bioconcentration test
Principal investigator: Dr. Heather A. Leslie, VU University, Netherlands

ECO 11: Influence of microbial biomass and diversity on biotransformation
Principal investigator: Dr. Russell Davenport, University of Newcastle, UK

ECO 13: Applying and verifying PBT/POP models through comprehensive screening of chemicals (completed)
Principal investigator: Prof. Michael McLachlan, Stockholm University, Sweden

ECO 17: Evaluation of test methods for measuring toxicity to sediment organisms
Principal investigator: Prof. Albert Koelmans, Wageningen University, Netherlands

ECO 18: Identifying limitations of the OCED water-sediment test (OECD 308) and developing suitable alternatives to assess persistence
Principal investigator: Dr Kathrin Fenner, EAWAG, Department of Environmental Chemistry, Switzerland

ECO 19: Towards more ecologically realistic assessment of chemicals in the environment *
Principal investigator: Dr. Frederik De Laender, Ghent University, Belgium

ECO 20: Development of an alternative testing strategy for the fish early life-stage (FELS) test (OECD 210) *
Principal investigator: Prof. Dr. Dries Knapen, University of Antwerp, Belgium

ECO 21: Mechanistic Bioaccumulation Model(s) for Ionogenic Organic Substances in Fish *
Principal investigator: Dr. Jon Arnot, ARC Arnot Research & Consulting Inc, Canada

Acceptance of new technologies and products

ECO 14b: Development and validation of an abbreviated in vivo fish bioconcentration test
Principal investigator: Dr. Duane Huggett, University of North Texas, USA

ECO 15: Rapid estimation of TMF using laboratory, field and computer modelling methods in aquatic organisms
Principal investigator: Prof. Michael McLachlan, Stockholm University, Sweden

ECO 16: Critical body residue validation for aquatic organisms exposed to chemicals causing toxicity by baseline narcosis
Principal investigator: Dr. Joop Hermens, University of Utrecht, Netherlands

N2: Assessment of nanoparticle specific effects in environmental toxicity testing (Complete but now leading to a Workshop)
Principal investigator: Dr. Alistair Boxall, University of York, UK

Impact of complex environments on health

ECO 6.2a: Establishing relationships of biotransformation across organisms (completed)
Principal investigator: Dr. Alistair Boxall, University of York, UK

EMSG 55: Critical evaluation of individual and combined natural and synthetic endocrine active compounds in fish: an in vitro & in vivo approach
Principal investigator: Prof. Tom Hutchinson, CEFAS, UK

COMMUNICATION

Publications

ECETOC's primary outputs are state-of-the-science reviews that are compiled as a result of the scientific partnerships formed in the framework of ad-hoc issues-based task forces. These take the form of both ECETOC's own published reports and the articles published in in the open scientific literature.

Technical Reports address specific aspects of the science used in evaluating the hazards and risks of chemicals to human health and the environment. (Note: Since 2009, 'Monographs', which were comprehensive reviews of generic topics or issues fundamental to the application of good science in evaluating the hazards and risks of chemicals, and 'Documents', which were scientific briefing papers addressing emerging issues, are also published as Technical Reports.

Workshop Reports are summaries of the discussions and conclusions derived from ECETOC sponsored scientific workshops.

Scientific Articles are publications in peer-reviewed journals.

JACC Reports (Joint Assessment of Commodity Chemicals) are comprehensive reviews of all available toxicological and ecotoxicological data on specific chemical substances, predominantly those having widespread and multiple uses. Each report presents a hazard assessment and identifies gaps in knowledge. The standard format may be extended in support of EU or other international risk assessment, or setting of an occupational exposure limit value.

Special Reports are compilations of data targeted to specific regulatory issues/demands.

Please note that, as part of our continuing drive for efficiency and environmental care, all ECETOC publications are now distributed exclusively in electronic format. All reports can be freely downloaded from http://www.ecetoc.org/publications

Reports published by ECETOC

Technical Reports

No. 114 ECETOC TRA version 3: Background and rationale for the improvements (Published July 2012)

No. 115 Effects of chemical co-exposures at doses relevant for human safety assessments (Published July 2012)

No. 116 Category approaches, read-across, (Q)SAR (Published November 2012)

Workshop Report

No. 23 Epigenetics and chemical safety. 5-6 December 2011, Rome (Published May 2012)

2012 Articles published in the open scientific literature

Bars R, Fegert I, Gross M, Lewis D, Weltje L, Weyers A, Wheeler JR, Galay-Burgos M.
Risk assessment of endocrine active chemicals: Identifying chemicals of regulatory concern.
Regulatory Toxicology and Pharmacology. 64(1):143-154 Doi:10.1016/j.yrtph.2012.06.013


Awarded 'Best Published Paper Advancing the Science of Risk Assessment' by the American Society of Toxicology (SOT) Risk Assessment Specialty Section (RASS)

The paper was published in the Regulatory Toxicology and Pharmacology Journal in 2012 and can be accessed here: http://bit.ly/ecetoc-art-2012-raeac. It builds upon an earlier paper published in 2011 in the same journal.

van Ravenzwaay B, Brunborg G, Kleinjans J, Galay Burgos M, Vrijhof H.
Use of 'Omics to Elucidate Mechanism of Action and Integration of 'Omics in a Systems Biology Concept.
Mutation Research - Genetic Toxicology and Environmental Mutagenesis 476(2)
Doi: 10.1016/j.mrgentox.2012.04.004

Hennes EC.
An overview of values for the threshold of toxicological concern.
Toxicology Letters 211(3):296–303 Doi: 10.1016/j.toxlet.2012.03.795

Hennes EC, Galay Burgos M, Hamer M, Pemberton M, Travis K, Rodriguez C.
Workshop: Combined exposure to chemicals.
Regulatory Toxicology and Pharmacology 63:53-54 Doi: 10.1016/j.yrtph.2012.02.008

Lavelle KS, Schnatter RA, Travis KZ, Swaen GM, Pallapies D, Money C, Priem P, Vrijhof H.
Framework for integrating human and animal data in chemical risk assessment.
Regulatory Toxicology and Pharmacology 62:302-312 Doi: 10.1016/j.yrtph.2011.10.009

Communication

Online communication

During 2012, ECETOC concentrated on refining the members' web site and the recently-developed joint editing platform that streamlines the creation of reports by task forces.

The social media linked to the public website, such as Twitter, LinkedIn and ResearchGate, gained in popularity with those who like to be kept informed of the latest news and developments from ECETOC. Follow ECETOC at:

External representation

Representation at specific meetings and input to specific projects and reports

5th SETAC Europe Special Science Symposium
15-16 February 2012, Brussels, Belgium
ECETOC was represented by Malyka Galay Burgos (ECETOC)

Workshop on utilisation of ecotoxicological research in society - bridging the gap between scientists and stakeholders
1 March 2012, Gothenburg, Sweden
ECETOC was represented by Malyka Galay Burgos (ECETOC)

WHO Workshop on 'Risk Assessment Methodologies'
28 March 2012, Bonn, Germany
ECETOC was represented by Henk Vrijhof (ECETOC)

BAuA / BfR Workshop: Non-endocrine disrupting human health hazards leading to SVHC identification
29 March 2012, Berlin, Germany
ECETOC was represented by Edgar Leibold (BASF), Giuseppe Malinverno (Solvay) and Volker Soballa (Evonik)

EU-funded Joint Action NanoGenotox – Stakeholder Workshop
3 May 2012, Brussels, Belgium
ECETOC was represented by Markus Schulz (BASF) and Henk Vrijhof (ECETOC)

ECHA Workshop on Nanomaterials
30-31 May 2012, Helsinki, Finland
ECETOC was represented through Marie-Louise Meisters (DuPont)

ECHA Workshop: Scientific Adequacy of in vivo Mutagenicity Assays, the Transgenic Rodent Gene Mutation Assay and the Unscheduled DNA Synthesis Assay
4 October 2012, Helsinki, Finland
ECETOC was represented by Ewan Booth (Syngenta) who industry perspective on UDS and TGR assays

SETAC Europe 6th Special Science Symposium
24-25 October 2012, Brussels, Belgium
ECETOC was represented by Malyka Galay Burgos (ECETOC)

ECHA Stakeholder Workshop
22 November 2012
ECETOC was represented by Christa Hennes (ECETOC)

Endocrine Disrupter Ad-Hoc meeting EU Commission
30 November 2012, Brussels, Belgium
ECETOC was represented by Malyka Galay Burgos (ECETOC)

6th Framework Programme Co-ordination Action Project "Norman"
Participation in Advisory Board on behalf of ECETOC by Stuart Marshall (Unilever)

7th Framework Programme Co-ordination Action Project "EUROECOTOX"
Malyka Galay Burgos (ECETOC) is the partner of the project for ECETOC. She also participated in the 1st European conference on the replacement, reduction and refinement of animal experiments in ecotoxicology, held 28-29 June 2012 in Dübendorf, Switzerland, and the final project meeting held 1-2 October 2012 in Brno, Czech Republic. Several reports have now been published.

DG SANCO Scientific Committees Discussion Paper on 'New Challenges for Risk Assessment'
With input from scientists in the ECETOC membership, comments have been submitted to the public consultation.

ILSI Europe Environment and Health Task Force
Participation on behalf of ECETOC by Malyka Galay Burgos (ECETOC)

Klimisch Update for Environmental Risk Assessment
With input from scientists in the ECETOC membership, the ring test has been evaluated and commented. The outcome of this exercise was presented at a special workshop at SETAC Glasgow 2013 and will be published soon. Several publications, including a peer reviewed paper, a book and several reports will be available in the near future.

STFC / NERC Bioinformatics and Environmental 'Omics Network
The overarching objective of the network is to build bridges between scientific communities in bioinformatics and environmental 'omics. The network will be co-aligned with the establishment of the new NERC Environmental 'Omics Synthesis Centre (EOS), which has the remit of exploring emerging areas of bioinformatics and environmental 'omics and their application to environmental problems. ECETOC is represented by Malyka Galay Burgos.

Representation in standing expert groups

Endocrine Disrupter Expert Advisory Group to the EU Commission (ED EAG)
Participation on behalf of ECETOC by Remi Bars (Bayer) and James Wheeler (Syngenta)

ECHA Risk Assessment Committee (RAC)
Participation as an observer on behalf of ECETOC by Alan Poole / Christa Hennes

ECHA Member State Committee (MSC)
Participation as an observer on behalf of ECETOC by Alan Poole / Christa Hennes

ECHA Partner Experts Groups (PEGs)
17 industry experts registered through ECETOC (Christa Hennes)

ECHA PBT Expert Group
Participation on behalf of ECETOC by Sylvia Jacobi (Albemarle)

ECHA Nanomaterials Working Group
Participation on behalf of ECETOC by Karin Wiench (BASF)

ECVAM Stakeholder Forum (ESTAF)
Participation on behalf of ECETOC by Remi Bars (Bayer)

OECD Working Party on Manufactured Nanomaterials
ECETOC was represented (via BIAC) by Hans-Jürgen Wiegand (Evonik)

WHO/IPCS Chemical Risk Assessment Network
Participation on behalf of ECETOC by Ben van Ravenzwaay (BASF)

Communication • External representation

Presentations and Posters

51st Annual Meeting of the Society of Toxicology (SOT)
11-15 March 2012, San Francisco, CA, USA
ECETOC Poster: *Evaluation of mixture effects at doses relevant for human safety*
Kim Travis (Syngenta), Alexius Freyberger (Bayer Healthcare), Majorke Heneweer (Shell), Christa Hennes (ECETOC), Heli Hollnagel (Dow), Hans Ketelslegers (ExxonMobil), Marie-Louise Meisters (DuPont), Stephanie Melching-Kollmuss (BASF), Nissanka Rajapakse (BP), Helen Tinwell (BayerCropscience), Martin Wilks (University Basel), presented by Marjoke Heneweer (Shell)

6th SETAC World Congress / SETAC Europe 22nd Annual Meeting
20-24 May 2012 Berlin, Germany
ECETOC Poster Part I: *Understanding the relationship between extraction technique and bioavailability.*
Charles Eadsforth (Shell), Helen Noble (AstraZeneca), Dan Letinski (ExxonMobil), Robin Oliver (Syngenta), Markus Telscher (Bayer), Tom Austin (Shell), Malyka Galay Burgos (ECETOC)

ECETOC Poster Part II: *Development of interim guidance for the inclusion of non-extractable residues (NER) in the risk assessment of chemicals*.
Gary Roberts (AstraZeneca), Chris Finnegan (Unilever), Gordon Sanders (Givaudan), Jay Worden (Shell), Martin Holt (ECETOC), Malyka Galay Burgos (ECETOC)

MEMBERS OF THE SCIENTIFIC COMMITTEE

Fraser Lewis (Chairman)	Syngenta
Ben van Ravenzwaay (Vice Chairman)	BASF
Remi Bars	Bayer CropScience
David Farrar[a]	INEOS ChlorVinyls
Andreas Flückiger	F. Hoffmann-La Roche
Helmut Greim	Technical University Munich
Guiseppe Malinverno	Solvay
Lorraine Maltby	University of Sheffield
Stuart Marshall	Unilever
Marie-Louise Meisters	DuPont
Chris Money	ExxonMobil Petroleum & Chemical
Mark Pemberton	Systox Limited (Formerly of Lucite)
Carlos Rodriguez	Procter & Gamble
Leslie Rushton	Imperial College London
Dan Salvito	RIFM on behalf of IFF
Jason Snape	AstraZeneca
Gerard Swaen	Dow Chemical
Johannes Tolls	Henkel
Saskia van der Vies	VU University Medical Center
Kees van Leeuwen	KWR Watercycle Research Institute
Hans-Jürgen Wiegand	Evonik Industries

[a] **Retired at the end of 2012**

MEMBERS OF THE SECRETARIAT

Alan Poole	Secretary General
Christa Hennes	Health Sciences Manager
Henk Vrijhof	Chemicals Programme Manager
Malyka Galay-Burgos	Environmental Sciences Manager
Geneviève Gérits	Office Manager
Ian Cummings	Communications, Web & Media Manager
Christine Yannakas	Administrative Assistant
Sonia Pulinckx	Administrative Assistant

The ECETOC Secretariat is responsible for the co-ordination and management of the scientific work programme, ensuring that the tasks assigned by the Scientific Committee are accomplished in a timely fashion. ECETOC's continued success relies greatly on its Secretariat. This team of dedicated professionals supports the scientists engaged in the work of the ECETOC programme in meeting the objectives set by the Scientific Committee.

On 1st October 2012, Dr Alan Poole, previously of Dow Europe, succeeded Dr Neil Carmichael as Secretary General of ECETOC. Neil Carmichael retired from ECETOC after 30 years in the chemical industry. His association with ECETOC goes back to 1983. He was a member of the Scientific Committee from 1990-2003 and became Secretary General in November 2006. During his time as Secretary General, Neil established ECETOC as a leading organisation in developing scientific answers and new approaches for important challenges in the areas of Toxicology and Ecotoxicology. This has increased the importance of ECETOC in supporting scientific and regulatory development not only in Europe but also internationally, and also its understanding within the industry.

Alan Poole obtained his B.Sc. in Biochemistry from the University of Cardiff and his PhD from the University of Surrey. He is a Fellow of the Royal College of Pathologists. He worked for the Medical Research Council in the UK studying the modes of action of pulmonary lung carcinogenesis, in particular mesothelioma, before moving to Smith Kline and French to lead a scientific team involved in preclinical development of ethical pharmaceuticals. He was later employed by Dow Chemical in Switzerland, where he worked for over 20 years addressing safety of industrial chemicals, during which time he participated in many industry and governmental activities. He has authored a book on toxicology as well contributing chapters to several others, and has published widely in the scientific literature.

FINANCE

INCOME ACTUAL 2012 IN EURO	
Subscription	
39 Full Members	1,242,000
6 Associate Members	70,000
Total Subscription Income	1,312,000
Bank Interest	12,121
Investment income	10,968
Project-related	244,009
Total	**1,579,098**

EXPENDITURE ACTUAL 2012 IN EURO	
Salaries (and related expenses)	968,447
Office Running Expenses	209,738
Travel Expenses on Missions	17,188
Meetings and Consultants	335,459
Professional Services	12,432
Bank Charges	4,859
Capital Expenditure	5,054
Publications	20,571
Miscellaneous	19,424
Website	8,487
Total	**1,601,659**

BALANCE SHEET AND RESERVES ACTUAL 2012 IN EURO	
Balance Sheet	
Income	1,579,098
Expenditure	1,601,659
Operating Margin	-22,561
Reserves*	
Opening	2,014,015
Operating Margin	-22,561
Closing Reserves	**1,991,454**

*Estimated Reserve Required 400,000

ABBREVIATIONS

(Q)SAR
(Quantitative) structure-activity relationships

µRNA
MicroRNA

3Rs
Replacement, refinement and reduction of animals in research

AR
Androgen receptor

ATM
Annual technical meeting

BAuA
German Federal Institute for Occupational Safety and Health

BfR
German Federal Institute for Risk Assessment

Chesar
Chemical safety and report tool

C&L
Classification and labelling

CAR
Constitutive androstane receptor

CEFIC
European Chemical Industry Council

CLP
Classification, labelling and packaging

CSA
Chemicals Safety Assessment

DG SANCO
Directorate General for Health & Consumers

DNA
Deoxyribonucleic acid

EA
Environment Agency

ECETOC
European Centre for Ecotoxicology and Toxicology of Chemicals

ECHA
European Chemicals Agency

ECVAM
European Centre for the Validation of Alternative Methods

ED EAG
Endocrine Disrupter Expert Advisory Group to the EU Commission

EDC
Endocrine disrupting chemical

EEMS
European Environmental Mutagen Society

EFSA
European Food Safety Authority

EOS
NERC Environmental 'Omics Synthesis Centre

ER
Estrogen receptor

ERLT
Environment research liaison teams

ESTAF
ECVAM Stakeholder Forum

ESTIV
European Society of Toxicology in Vitro

EU
European Union

EUROECOTOX
European Network for Alternative Testing Strategies in Ecotoxicology

EUROSTAT
Statistical office of the European Union

EUROTOX
Association of European Toxicologists and European Societies of Toxicology

EUSES
European unified system for the evaluation of substances

HEMT
Health effects monitoring team

HETRA
Human exposure and tiered risk assessment

IPCS
International Programme on Chemical Safety

INSERM
Institut National de la Santé et de la Recherche Médicale, Nice

IR
Information requirements

LRI
Cefic's Long-range Research Initiative

mRNA
Messenger RNA

MSC
(ECHA) Member State Committee

NER
Non-extractable residues

NERC
Natural Environment Research Council UK

NO(A)EL
No observed adverse effect level

OECD
Organisation for Economic Co-operation and Development

PBT
Persistent, bioaccumulative toxic

PEG
(ECHA) Partner Expert Group

POP
Persistent organic pollutant

PPAR
Peroxisome proliferator activated receptor

PXR
Pregnane X receptor

RAC
(ECHA) Risk Assessment Committee

REACH
EU regulatory framework for the registration, evaluation and authorisation of chemicals

RfP
Request for proposal

RNA
Ribonucleic acid

SC
Scientific Committee

SETAC
Society of Environmental Toxicology and Chemistry

SIG
LRI strategy implementation group

SOT
US Society of Toxicology

SpERCs
Specific Environmental Release Categories

STFC
Science and Technology Facilities Council, UK

SVHC
Substance of very high concern

TAGs
Tiered aggregate exposure to chemical substances

TET
Ten eleven translocation

TGR
Transgenic rodent

TR
ECETOC technical report

TRA
Targeted risk assessment

UBA
Federal Environment Agency of Germany

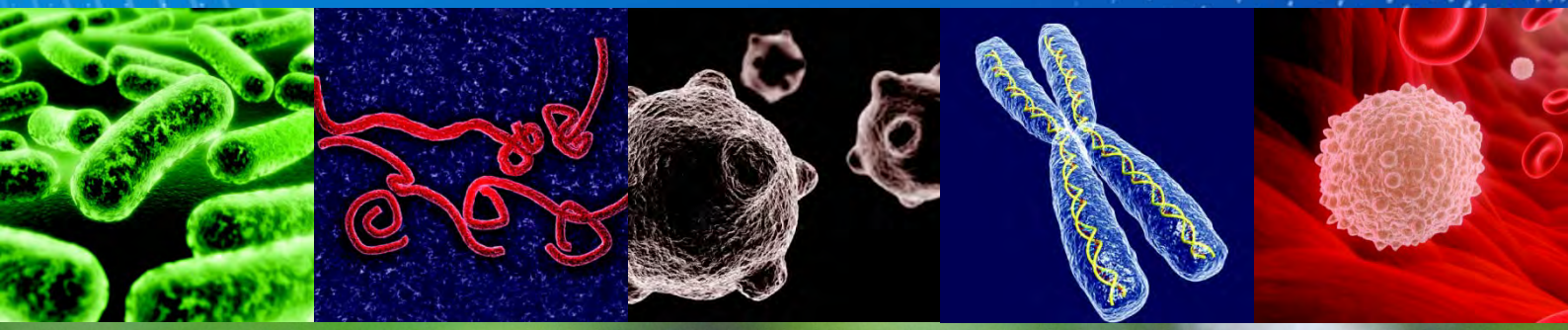
UDS
Unscheduled DNA synthesis

UVCB
Substances of unknown or variable composition

WHO
World Health Organisation

WR
ECETOC workshop report

X2012
7th International Conference on the Science of Exposure Assessment



Established in 1978, ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.

ECETOC AISBL

Av. E. Van Nieuwenhuyse 2 (Bte 8)
B-1160 Brussels, Belgium
Tel: (32) 2 675 3600
Fax: (32) 2 675 3625
Email: info@ecetoc.org
Website: www.ecetoc.org
VAT: BE 0418344469